REMARKS

The Official Action has objected to Claims 5, 15, 58-62 and 79-83, but has indicated that the subject matter therein is allowable if rewritten in independent form. However, it rejected Claim 8 under 35 USC §112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In addition, it has rejected Claims 1, 2, 6, 8, and 56 under 35 USC §102(b) as defining subject matter which is allegedly anticipated by the teachings in U.S. Patent No. 4,707,468 to Yoshino, et al. ("Yoshino, et al."). Further Claims 1, 2, 8, 16-19, 51, 56 and 73 are rejected under 35 USC §102(b) as defining subject matter which is allegedly anticipated by the teachings in U.S. Patent No. 4,510,082 to Gesellchen, et al. ("Gesellchen, et al."). Further, Claims 1, 2, 8, 16-19, 73 and 75 are rejected under 35 USC §102(b) as defining subject matter which is allegedly anticipated by the teachings of EP 997,147, to which Seko, et al. are inventors ("Seko, et al."). Claims 1, 2, 8, 16-19 and 73 are further rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of U.S. Patent No. 6,180,611 to Montana, et al. ("Montana, et al."). Further, Claims 1, 2, 8, 16-19 and 73 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Montana, et al. in view of an article by Konttinen, et al., in Arthritis and Rheumatism, 37(7) 965-82, (1994) ("Konttinen, et al."). Moreover, Claims 1, 2, 16-19, 73, 77 and 78 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of U.S. Patent No. 4,518,587 to Laruelle, et al. ("Laruelle, et al."). In addition, Claims 1, 2, 6, 8, 16-19, 73, 74, and 78 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of U.S. Patent No.6,737,408 to Balasubramanium, et al. ("Balasubramanium, et al."). Moreover, Claims 1, 2, 6, 8-10, 14, 16-19, 51, 56, 73-75 are

rejected under 35 §103 as defining subject matter which is allegedly rendered obvious by the teachings of U.S. Patent No. 4,533,657 to Morgan ("Morgan"). In addition, Claims 1, 2, 6, 16-19, 73 and 74 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of U.S. Patent No. 5,508,266 to Fink ("Fink"). Claims 1, 2, 16-19, 75 and 76 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of U.S. Patent No. 6,037,324 to Schwender, et al. ("Schwender, et al."). Claims 1, 2, 16-19 and 73 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of U.S. Patent No. 6,126,939 to Eisenbach-Schwartz, et al. ("Eisenbach-Schwartz, et al."). Claims 1, 2, 6, 8, 16, 18, 73 and 56 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Yoshino, et al. in view of Lowry, Mechanism and Theory in Organic Chemistry, Harper & Row, pp. 60-70 (1976) ("Lowry"). In addition, Claims 1, 2, 8, 16-19, 51, 56, and 73 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Gesellchen, et al. in view of Lowry. In addition, Claims 1, 2, 8, 16-19, 73 and 75 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Seko, et al. in view of Lowry. Moreover, Claims 1, 2, 8, 16-19, and 73 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Montana, et al. in view of Lowry. Further, Claims 1, 2, 8, 16-19 and 73 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Montana, et al. in view of Konttinen and further in view of Lowry. Claims 1, 2, 16-19, 73, 77 and 78 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Laruelle, et al. in view of Lowry. Claims 1, 2, 6, 8, 16-19, 73, 74 and 78 are rejected under 35 USC §103 as defining

subject matter which is allegedly rendered obvious by the teachings of Balasubramanium, et al. in view of Lowry. Claims 1, 2, 6, 8-10, 14, 16-19, 51, 56 and 73-75 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Morgan, et al. in view of Lowry. In addition, Claims 1, 2, 6, 16-19, 73 and 74 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Fink in view of Lowry. Further, Claims 1, 2, 16-19, 75 and 76 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Schwender, et al. in view of Lowry. Finally, Claims 1, 2, 16-19 and 73 are rejected under 35 USC §103 as defining subject matter which is allegedly rendered obvious by the teachings of Eisenbach-Schwartz, et al. in view of Lowry.

Applicant has amended the claims which, when considered with the comments herein, are deemed to place the present case in condition for allowance. Favorable action is respectfully requested.

Before addressing the merits, it should be noted that applicant has amended Claim 1 by specifically reciting the electron withdrawing groups and electron donating groups therein for R and R_1. Support for the amendment to Claim 1 is found on Page 20, lines 7-31 of the instant specification. In view of this amendment, R and R_1 cannot include peptides or other amino acids. Further Claim 1 has been amended to restrict the scope thereof to R being aryl lower alkyl, which may be unsubstituted or substituted on the aryl moiety with an electron withdrawing group or electron donating group and R_1 being lower alkyl which may be unsubstituted or substituted with an electron withdrawing group or electron donating group. Support is found on page 25, line 31 to page 26, line 12 of the instant specification. The definitions of R_2 and R_3 have also been narrowed. Support is found on page 15, line 26 to page 17, line 29, page 23, line 1 to

page 25, line 30 of the instant specification. Claims 6-9 have been amended and are directed to preferred embodiments.

This narrowing of the claims was effected for reasons unrelated to patentability; they were effected to minimize fees and to direct the claimed subject matter to embodiments which have commercial potential.

Applicant has also added Claims 90-107 to the instant application. Support for Claims 90-107 is found on page 20, line 1 to page 23, line 23 and page 24, line 3 and page 27, line 10 of the instant application.

These amendments also deleted subject matter. Applicants have not abandoned this subject matter and reserve the right to file a continuation application directed thereto.

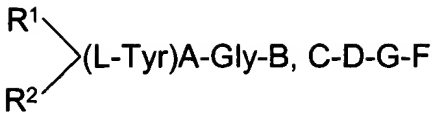
No new matter is added to the application.

Pursuant to the rejection of Claim 8, under 35 USC §112, second paragraph, the Office Action alleges that there is no antecedent basis in Claim 6 for the substituents to be substituted by electron withdrawing or an electron donating group. To rectify that problem, Claim 8 has been amended to be dependent upon Claim 1, which recited that R_3 may be unsubstituted or substituted with an electron donating group or electron withdrawing group. Thus, there is antecedent basis for the language in Claim 8. Therefore, the rejection of Claim 8 under 35 USC §112, second paragraph is obviated, withdrawal thereof is respectfully requested.

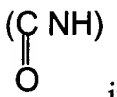
Pursuant to the rejection of Claims 1, 2, 6, 8, and 56 under 35 USC §102(b) the Office Action cites Yoshino, et al.

Yoshino, et al. does not teach, disclose or suggest the present invention.

Yoshino, et al. disclose a linear peptide of the formula



In other words, Yoshino, et al. is comprised of a linear polypeptide containing at least 6 linear amide linkages. It does not disclose any compounds having only 2 linear amide linkages



in the main chain, the subject matter of the present application. As amended, the compounds described in the rejected claims of the present invention cannot contain any amide linkages in either R or R_1. A review of the definitions of the electron donating groups and electron withdrawing groups recited in Claim 1 clearly reveals that these groups do not include amide functionalities. Accordingly, the compounds used in the present invention cannot possess any peptide linkages in R and R_1. Thus, there are only 2 linear amide linkage in the compounds utilized in the present invention and they are the two linear amide linkages depicted in the main chain.

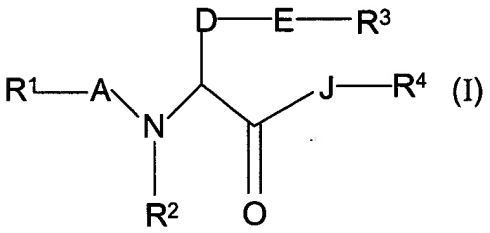
Anticipation requires identity of invention; a finding of anticipation requires that the publication describes all of the elements of the claims. See, for example, Continental Can Co., USA Inc. v. Monsanto Co., 948 F2d 1264, 1267, 20 USPQ 2d 1746, 1748 (Fed Cir 1991); In re Spada, 911 F2d 705, 708, 15 USPQ 2d 1655, 1657 (Fed Cir 1990).

Inasmuch as Yoshino, et al. does not disclose any compounds therein for treating pain having only 2 linear amide linkages in the main chain, it does not teach, disclose or suggest the use of the compounds of the present invention. Thus, the rejection of Claims 1, 2, 6, 8 and 56 under 35 USC §102(b) is obviated, withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 1, 2, 8, 16-19, 51, 56 and 73 under 35 USC §102(b), the Office Action cites Gesellchen, et al.

Gesellchen, et al. disclose a compound comprising at least three amide bonds in a linear chain. The three amide bonds are: one between Tyr and A, one between A and Gly and one between Gly and NR_1. It does not teach, describe or suggest a compound for treating pain having only two linear amide linkages in the main chain, as claimed. As defined and indicated hereinabove, R and R_1 herein cannot include any amide functionalities. Thus, Gesellchen, et al. do not teach, disclose or suggest the subject matter in Claim 1, 2, 8, 16-19, 51, 56 and 73. Therefore, this rejection under 35 USC §102(b) is obviated; withdrawal thereof is respectfully requested.

Seko, et al. disclose compounds of the formula



The Office Action refers to the compounds disclosed on Pages 24-27 and alleges that the examples therein encompass compounds using the nomenclature in the present application, wherein R is benzyl substituted with EWG/EDG, R_1 is alkyl substituted by EWG/EDG, R_2 is hydrogen and R_3 is methyl substituted by cyclopentylmethyloxy and concludes that these compounds anticipate the subject matter of the present invention.

Applicants disagree that the exemplification on pages 24-27, anticipate the subject matter in the rejected claims. There are many differences between the exemplified compounds on pages 24-27 of Seko, et al. and the compounds utilized in the method of the present invention. For example, contrary to the allegations in the Office Action, the substituent R_1, which according to the Office Action corresponds to R_1 of the compounds used in the present invention, is not an

alkyl group substituted with EWG/EDG. The R_1 substituent shown in Seko, et al. on pages 24-27 does not have an alkylene group therein, as alleged in the Office Action. The R_1 substituents on pages 24-27 of Seko, et al. are connected to the acyl group by a cyclic structure, e.g., cycloalkyl, heterocyclic, aromatic or heteoaryl groups such as, phenyl, cyclohexyl, oxazoyl, furyl, imidazolyl, thiazolyl, thenyl, and the like. As depicted in Seko, et al. in R_1 the line drawn attached to the ring indicates the point of attachment of the cyclic group to the acyl group on the main chain and not an alkylene group. On the other hand, in the compounds described in the present invention, the R_1 group (i.e., the group attached to the acyl group) is not a cyclic structure as in the examples of Seko, et al., but is instead an alkyl group, e.g., methyl, which may be unsubstituted or substituted. Since the exemplification on pages 24-27 of Seko, et al., do not disclose a bridging alkylene group in the definition of R_1 separating the acyl group from the cyclic moiety, and since, as claimed, the present invention requires that R_1 be an alkyl group which may optionally be substituted, the exemplification on pages 24-27 of Seko, et al. do not teach disclose or suggest the present invention.

A quick review of the remaining exemplification clearly shows that none of the examples teach or disclose the compounds recited in the rejected claims. More specifically, none of the examples describe a group containing two linear amide groups wherein R_1 is alkyl, R is arylalkyl, which R and R_1 groups can be unsubstituted or substituted, as defined and R_2 and R_3 are as defined herein with the specific electron withdrawing groups and electron donating as specified in Claim 1 and those dependent thereon.

Moreover, a quick review of the exemplification also reveals that none of the examples teach or disclose the subject matter of Claims 90 et seq. None of the exemplifications teach or disclose compounds containing two linear amide compounds wherein R_1 is methyl, which is

unsubstituted or substituted, R is aryl lower alkyl which is unsubstituted or substituted and R_2 and R_3 are as defined.

Further, the general teachings of Seko, et al. do not teach or disclose the present invention. As indicated hereinabove, anticipation requires identity of invention, i.e., the prior art reference must teach or disclose the claimed subject matter. However, the generic formula disclosed in Seko, et al. is so broad that it covers thousands and thousands of compounds. Even assuming, pro arguendo, that there was some overlap between the generic formula and the compounds utilized in the rejected claims or Claims 90 et seq., to which applicants are not making any such admission, that still does not mean that the teachings of Seko, et al. anticipate the present invention. Under those circumstances, case law has held that when a compound is not specifically named in a prior art reference but, can be obtained by selecting particular portions of the reference and selecting various substituents from a list of alternatives, anticipation can only be found if the classes of substituents are sufficiently limited and well delineated. Ex parte A, 17 USP02d 1716, (Bd. Pat. App. & Inter, 1990). However, even assuming, pro arguendo, there were overlap of the compounds used in the present invention with the compounds described in Seko, et al., the teachings in Seko, et al. encompass thousands and thousands of compounds and is not directed to a limited class of compounds that are identifiable. There is no teaching or suggestion therein that would lead one of ordinary skill in the art to the specific genus claimed even if there was overlap between the teachings of Seko, et al. and the present invention. The situation at hand is more akin to that in In re Meyer, 599F2d 102, 202 USPQ 175 (CCPA 1979). In Meyer, the claims were directed to an alkali hypochlorite. A cited reference disclosed an alkaline chlorine or bromine solution; the United States Patent and Trademark Office alleged that the reference anticipated the invention. The Meyer Court held

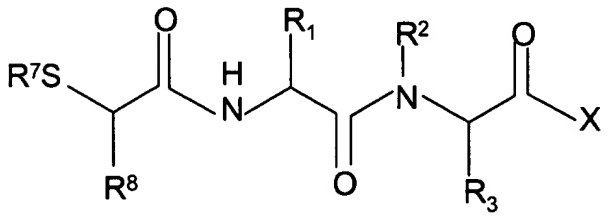
that the genus, alkaline chlorine or bromine solution does not identically disclose describe the species alkali metal hypochlorite, since the genus includes an untold number of species.

This is similar to the situation herein since Seko, et al. disclose an untold number of species, and since there is nothing specific therein that would point to the specific combination and permutations that when correctly selected would disclose or describe the claimed genus of the present invention.

Therefore, for the reasons given, this rejection of Claims 1, 2, 8, 16-19, 73 and 75 under 35 U.S.C. §102(b) is obviated, withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 1, 2, 8, 16-19 and 73 under 35 USC §103, the Office Action cited Montana.

Montana discloses compounds of the formula



wherein X is N R^4R^5. Montana, et al. require that the compound contains three linear amide bonds.

The Office Action further refers to Ex 71, which is directed to N-[2-Mercapto-4-succinimidobutanoyl-]-L-(O-methyl) serinyl-L-tert-leucine-N-methyl amide.

Montana, et al. require the compounds to possess three linear amide linkages for there to be activity. However, as defined, the compounds used in the present invention have only two linear amide functionalities and still is active in treating pain. The prior art reference do not teach or disclose or suggest any compounds having less than three linear amide functionalities.

Thus, it is surprising that the present compounds have activity, despite the fact that it only has two linear amide functionalities. Thus, for the reasons given, the rejection of Claims 1, 2, 8, 16-19 and 73 under 35 USC §103(a) is obviated, withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 1, 2, 8, 16-19 and 73 under 35 USC §103, the Office Action cites Montana in view of Konttinen.

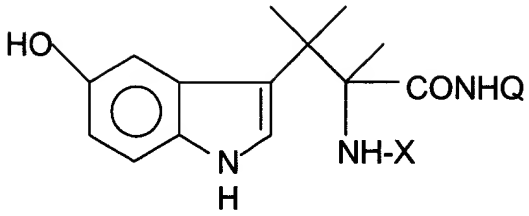
The Office Action reiterates the arguments presented above. It cites Montana, et al. for allegedly teaching that it is useful for treating arthritis. It cites Konttinen for its alleged teaching that there is pain associated with arthritis.

Applicant reiterates the arguments hereinabove with respect to Montana, et al. Konttinen, et al. do not overcome the deficiencies of the primary reference. It does not teach or disclose any peptides for treating pain. Moreover, it is being applied by the United States Patent and Trademark Office to show that pain "is associated with arthritis". Thus, even if there is pain associated with rheumatoid arthritis, which is the only arthritic disease disclosed in Montana, et al., Montana in combination with Kottinen, et al. does not teach or disclose the compounds used in the present invention. Thus, the combination at best would teach, disclose or suggest a compound having three linear amide linkages, and not just the two linear amide linkages, as claimed.

Therefore, for the reasons provided herein the rejection of Claims 1, 2, 8, 16-19 and 73 under 35 USC §103 is overcome; withdrawal thereof is respectfully requested.

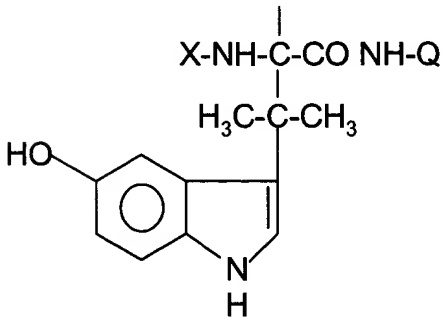
In support of the rejection of Claims 1, 2, 16-19, 73, 77 and 78 under 35 USC §103(c), the Office Action cites Laruelle, et al.

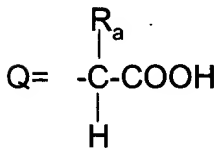
Laruelle, et al. disclose a dipeptide of L-5-hydroxytryptophan of the formula



in which X represents hydrogen or lower acyl radical and Q represents a free or esterified amino acid. According to the Office Action, Laruelle, et al. disclose that the compounds therein are useful analgesics. The Office Action cites a compound in Col. 7, line 45, viz, N-acetyl-5-(OH) Trp-Tyrosine and alleges that this compound falls within the scope of the compounds used in the present invention to treat pain.

Contrary to the allegations in the Office Action, none of the compounds in Laurelle, et al. fall within the scope of the compounds used in the present invention for treating pain. More specifically, contrary to the allegations in the Office Action, the substituent in Laruelle, et al.which is equivalent to R of the present invention is quite different and does not teach or suggest the definition of the R substituent in the present invention. To illustrate this, consider the compounds of to be written as follows





or ester thereof, Ra = side chain of an amino

X = H or loweracyl radical.

In this instance, Q of Laurelle, et al. corresponds to R of the present invention. But Q is an amino acid, i.e., in Ex. 71, it can be described as aralkyl substituent with a carboxy group or ester thereon. However, as defined, the R group of the compounds used in the present invention is not an amino acid moiety, for instance, it does not have a carboxy or carbalkoxy substituent thereon. Based on the teachings therein, it is surprising that compounds without the second amino acid moiety in NHR would have activity for treating pain. Further, unlike the referenced examples in Laurelle, et al., in which the COOH is substituted on the alkyl portion, in the claimed subject matter, the aryl group --and not the alkyl moiety-- contains the electron withdrawing or the electron donating group. Therefore, contrary to the allegations in the Office Action, the compounds of Laruelle, et al. does not fall within the scope of the present invention and do not suggest the compounds used in the present invention.

Thus, the teachings of Laruelle, et al. do not teach disclose or suggest the subject matter of Claims 1, 2, 16-19, 73, 77, 78, withdrawal of the rejection is respectfully requested.

Pursuant to the rejection of Claims 1, 2, 6, 8, 16-19, 73, 74 and 78, the Office Action cites Balasubramanium, et al.

Balasubramanium, et al. relates to dipeptides and tripeptides for control of appetite, blood pressure, cardiovascular responses, libido, and circadian rhythm. The Office Action cites in particular, the use of the compound Ac-Phe-Arg-Trp-NH_2.

As defined, contrary to the allegations in the Office Action this compound does not fall within the scope of Claim 1 as amended. The compound referred to by the Office Action is a linear tripeptide, that has four linear amide bonds, one between Ac and Phe, one between Phe and Arg, one between Trp and Arg and one between Trp and NH_2 (terminal). Balasubramanium, et al. do not teach, disclose or suggest a compound having two linear amide linkages as claimed.

Based on the teachings, it is quite surprising that a compound having only two linear amide bonds would be useful for treating pain. Thus, inasmuch as Balasubramanium, et al. do not teach, disclose or suggest compounds having two linear amide linkages, as claimed the cited art does not teach, disclose or suggest the present invention.

Consequently, for the reasons provided herein, the rejection of Claims 1, 2, 6, 8, 16-19, 73, 74 and 78 under 35 USC §103 is overcome; withdrawal thereof is respectfully requested.

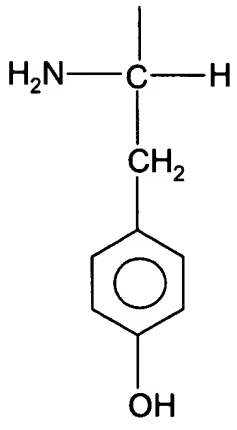
Pursuant to the rejection of Claims 1, 2, 6, 8-10, 14, 16-19, 51, 56, 73-75 under 35 USC §103, the Office Action cited Morgan.

According to the Office Action, Morgan discloses compounds for inducing analgesia. An example is

Tyr-D-Ala-NHCH(Me)-CH_2-CH_2-Ph

According to the Office Action, using the nomenclature described in the present invention, R is aryl loweralkyl, i.e., CH(Me)-CH_2-CH_2-Ph, R_2 is H, R_3 is CH_3, and R_1 is alkyl substituted with EWG/EDG, i.e., from the Tyrosine moiety.

In other words, using the nomenclature of the present invention, R_1 of Morgan is



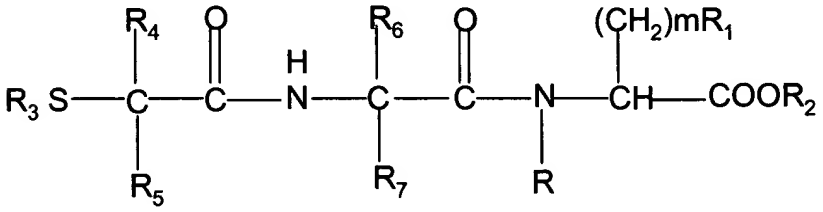
i.e., a tyrosine moiety without the carboxy group. However, the compounds used in the present invention do not include any tyrosine moieties. As defined, the only electron

withdrawing group and electron donating group are those specifically listed in the claims. As defined, the R and R_1 groups do not have amino, alkyl amino, dialkyamino or carboxy or carbalkoxy substituents thereon. Thus, unlike the compounds described in Morgan et al., the compounds used in the present invention do not have an amino acid for the group R or R_1. On the other hand, the R_1 group in the '657 patent is a tyrosine moiety without the carboxy group thereon, i.e., the alkyl group is substituted by an carboxy group. However, a review of the definition of R and R_1 clearly reveal that R cannot be substituted by and does not include carboxy derivative thereof. This Morgan et al. do not teach, disclose or suggest the use of the compounds recited in the rejected claims. Furthermore based on the teachings in Morgan, et al., it is surprising that a compound which does not contain an alkyl group substituted by carboxy at the R_1 position as presently claimed, would be useful for treating pain.

Thus, for the reasons given herein, the rejection of Claims 1, 2, 6, 8-10, 14, 16-19, 51, 56, 73-75 under 35 USC §103(a) is overcome, withdrawal thereof is respectfully requested.

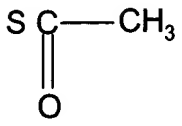
Pursuant to the rejection of Claims 1, 2, 6, 16-19, 73 and 74 under 35 USC §103, the Office Action cites Fink.

Fink discloses various compounds for treating pain. More specifically, it discloses compounds of the formula



The Office Action refers to the species disclosed in Column 14, line 45, wherein R_1 is 4-methoxyphenyl, R_2 is ethyl, R_3 is acetyl, R_4 is isopropyl, R_5 is hydrogen, R is H, and m is 1.

According to the Office Action, using the variables of the present claims, R_2 and R_3 are methyl, R_1 is lower alkyl substituted with



, and R is $CH(CH_2)mR_1$-$COOR_2$. Thus, R requires a carboxy or carbalkoxy substituent therein.

However, as defined in the rejected claims, R cannot have a carboxy or carbalkoxy substituent substituted thereon. A review of the electron donating groups and electron withdrawing groups defined by the present invention quickly reveals that it does not include carboxy or carbalkoxy. Further R, in the present claims is not defined to be substituted by methyl carbozythio, as in Fink. Thus, inasmuch as Fink requires the presence of these group on R and R_1 respectively, and inasmuch as the groups are not present on R and R_1, respectively, in the compounds used in the present invention, Fink does not suggest the compounds of the present invention. Moreover, it is surprising that the compounds of the present invention are useful for treating pain.

Pursuant to the rejection of Claims 1, 2, 16-19, 75 and 76 under 35 USC §103, the Office Action cites Schwender, et al.

Schwender, et al. is directed to the use of compounds useful for treating IBD. The Office Action cites two compounds, viz

Idc-Asp-Thr-NH-benzyl

Bpc-Asp-Thr-NH-benzyl,

wherein Idc is indolyl carbonyl and Bpc is benzofurancarbonyl.

According to the Office Action, there are two characterizations of the compounds of Schwender, et al. using the nomenclature of the present invention. The first one is, according to the Office Action,

R is benzyl;

R_2 is hydrogen;

R_3 is alkyl substituted with hydroxyl;

R_1 is alkyl substituted with EWG/EDG;

i.e., Asp without the ((CO) group attached to Idc or Bpc). It is to be noted that R_3 is the side chain of the threonine.

The second characterization is R_1 is a heterocyclic i.e., indole or Benzofuran, R_2 is hydrogen, R_3 is alkyl substituted with carboxyl (Asp), and R is alkyl substituted with EWG/EDG (i.e., Thr without the amino group attached to the –NH-benzyl).

Schwender, et al. do not teach, disclose or suggest the present invention. The compounds used in Schwender, et al. require three linear amide functionalities, one between Idc (or Bpc) and Asp, one between Asp and Thr and one between Thr and NH benzyl. However, as defined, the compounds of the present invention have only two linear amide functionalities. Thus, it is surprising that the compounds of the present invention are useful for treating pain without the additional linear amide functionality. Consequently, the use of the compound of the present invention for treating pain is surprising in view of the teachings of Schwender, et al. Thus, for the reasons given herein, the rejection of Claims 1, 2, 16-19, 75 and 76 under 35 USC §103 over Schwender, et al. is overcome; withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 1, 2, 16-19, and 73 under 35 USC §103, the Office Action cites Eisenbach -Schwartz, et al. It alleges that the various compounds therein are useful

for treating pain. Moreover, it alleges that the tripeptides listed in Col. 3, lines 48-61 are encompassed by Claim 1.

Applicants disagree that the tripeptides disclosed in Eisenbach-Schwartz, et al. are encompassed by the formula of the present invention. As defined, the compounds used in the present invention contain two amide functionalities of which only one can be part of an amino acid. Thus, the linear amide portion contains two less amino acids than that disclosed in Eisenbach-Schwartz. Eisenbach-Schwartz thus do not teach, disclose or suggest any other types of compounds except those containing at least two or more amino acids. Consequently, it does not teach, disclose or suggest the compounds of the present invention. Further, in view of these differences in structure , it is surprising that the compounds used in the present invention are useful for treating pain.

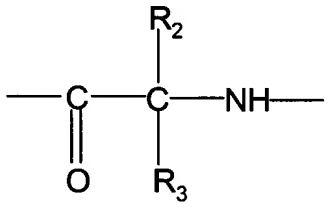
Thus, for the reasons given herein the rejection of Claims 1, 2, 16-19 and 73 under 35 USC §103(a) over Eisenbach-Schwartz, et al. is overcome, withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 1, 2, 6, 8, 16, 18, 56 and 73 under 35 U.S.C. §103 the Office Action combines Lowry, et al. with Yoshino, et al. It reiterates the arguments hereinabove with Yoshino, et al. However, as pointed out hereinabove, Yoshino, et al. disclose a polypeptide having at least 6 linear amide bonds from the 8 amino acids contained thereon. It does not teach, disclose or suggest that compounds like the present invention having 2 linear amide bonds can be used to treat pain.

Lowry does not overcome the deficiency of the primary reference. Lowry is being cited to show that certain groups are electron withdrawing groups while other groups are electron donating groups that there are electronically different from hydrogen. This teaching relates to

theoretical matters. Lowry et al. do not teach or suggest any compounds additional to those disclosed in the primary reference for treating pain. Thus, the teaching of Lowry et al. do not overcome the deficiencies described hereinabove with respect to Yoshino, et al. Thus, the rejection of the claims 1, 2, 6, 8, 16, 18, 56 and 73 as being unpatentable over Yoshino et al. in view of Lowry et al. is overcome; withdrawal thereof is respectfully requested. Withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 1, 2, 8, 16-19, 51, 56 and 73, under 35 USC §103, the Office Action cites Gesellchen, et al. in view of Lowry et al. The Office Action reiterates its commentary with respect to Gesellchen, et al.

As indicated hereinabove, Gesellchen, et al. do not teach, disclose or suggest the present invention. More specifically, Gesellchen, et al. disclose compounds containing at least three amino acids. On the other hand as defined, the compounds used in the present invention do not contain 3 linear amino acids. It is noted that as defined both R and R_1 do not include amino or carboxy or derivatives thereof. Thus, the compounds used in the present invention may have two linear amide functionalities but the aforementioned mentioned amide can contain at most one amino acid, viz,  . Since R_1 does not contain any amino group, $R_1C(O)$ of the present invention cannot be an amino acid. Moreover, since R-NH does not contain any carboxy group or derivative thereof, R-NH group is not an amino acid.

In Gesellchen, et al., the group corresponding to R_1 also contains an amino alkyl group. However, as defined, the compounds disclosed in the present invention do not have such groups

therein because the definition of R_1 does not include substituents having amino functionalities thereon. Thus, Gesellchen, et al. do not teach, disclose, or suggest any compounds without the aforementioned critical features. But, as indicated hereinabove, those features are not present in the compounds used in the present invention. Thus, Gesellchen, et al. do not teach, disclose or suggest the present invention.

Lowry, et al. do not overcome the deficiency of the primary references. More specifically, it does not teach, disclose or suggest any compounds in addition to those in Gesellchen, et al. Since Lowry, et al. do not add to the deficiencies described hereinabove, the combination of Gesellchen, et al. and Lowry, et al. do not teach, disclose or suggest the present invention. Therefore, the rejection of Claims 1, 2, 8, 10-19, 51,56 and 73 under 35 USC §103(a) is overcome; withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 1,2,8,10-19, 73 and 75 under 35 USC §103, the Office Action cites Seko, et al. in view of Lowry.

The Office Action reiterates the comments regarding the teachings of Seko, et al. when applying the '102 rejection. The Office Action alleges that the compounds on Pages 24-27 disclose compounds fully within the scope of the invention and conclude that the teachings of Seko, et al. overlap with the compounds of the present invention.

Applicants disagree. As indicated hereinabove, the compounds on Page 24-27 do not disclose compounds falling within the scope of the present invention. Using the nomenclature of the compounds disclosed in the present invention, the R_1 substituent in Seko, et al. corresponds to the position of R_1 in the compounds used in the present invention. However, unlike the compounds of the present invention, where R_1 is alkyl, substituted by specific electron withdrawing or electron denoting groups, R_1 in Seko, et al. in these examples is a cyclic group,

i.e., a heterocyclic, aryl, cycloalkyl a heteroaryl group. The line attached to the cyclic groups does not indicate a alkyl group, but instead indicates the point of attachment of the cyclic group therein to the acyl group. None of the compounds therein in the tables on the aforementioned pages or any of the other pages teach, disclose or suggest the compounds of the present invention Applicant reiterates the arguments hereinabove with respect to the differences between the compounds of the present invention are those in Seko, et al.

However, even assuming that there is some overlap with the compounds of the present invention, as alleged by the Office Action, which applicants do not admit, it is to be noted that Seko, et al. encompasses millions of compounds. Even the preferred embodiments encompass a large class of compounds. Attention is directed to Page 6, et seq. which disclose the generic formula of the compounds described therein. As clearly seen the formula encompasses a large genus, and there is no teaching or suggestion therein that would lead one of ordinary skill in the art to choose the correct combination and permutations of the eight variables therein with the various definitions to the genus of the compounds used in the present invention. Moreover, as indicated hereinabove, none of the examples fall within the scope of the claimed invention.

All of these differences teach one of ordinary skill in the art away from the present invention. Based upon the teaching in Seko, et al., there is no suggestion to make the compounds of the present invention. Thus, the subject matter of the rejected claims are not taught, disclosed or suggested by the prior art.

However, the United States Patent and Trademark office has posited that the subject matter of the present invention is encompassed by the prior art, and that the present invention is thus rendered obvious.

Applicant disagrees. Even if one, pro arguendo, agrees with the Office Action that the claimed subject matter is a member of the genus of the prior art, that, in and of itself, is not sufficient to render subject matter of the claims obvious. See, In re Jones, 958 F.2d 347, 350, 21 U.S.P.Q.2d 1941, 1943 (Fed. Cir. 1992); In re Baird, 16 F.3d 380, 382, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994).

In fact, assuming the facts are as alleged by the Office Action, In re Jones and In re Baird, have held that, even under circumstances where the genus of the prior art encompasses claimed subject matter, the United States Patent and Trademark Office has not made out a prima facie case of obviousness.

In Jones, the applicant was claiming the 2-(2'-aminoethoxy) ethanol salt of dicamba. The prior art disclosed a genus which included an infinite number of compounds and which encompassed the specific salt that was claimed, although it did not disclose the specific salt claimed by applicants. The United States Patent and Trademark Office rejected the claims, alleging that the species was a member of the genus of the prior art. The Board of Patent Appeals and Interferences ("Board") affirmed. However, the Jones Court reversed the Board; it held that even though the claimed salt is a member of the genus in the referenced patent, this does not, in and of itself, make the salt obvious. Jones, 958 F.2d at 350, 21 USPQ2d at 1943. It held that each case must be determined on its own set of facts. Id. In reaching its conclusion that the Jones invention was not obvious, the Court focused on the facts that the cited prior art reference disclosed a huge genus consisting of an infinite number of salts and that it did not specifically disclose the claimed salt in the list of preferred salts. Id. Moreover, the Court also held that the claimed salt was not structurally sufficiently similar to those salts specifically

disclosed in the reference. Id. Thus, the Court held that the United States Patent and Trademark Office did not make out a prima facie case of obviousness.

In re Baird had a similar set of facts to Jones. The claim in issue was directed to a toner comprising a binder resin which is a bisphenol A polyester containing an aliphatic dicarboxylic acid selected from succinic acid, glutaric acid and adipic acid. It was rejected over a prior art reference relating to developer compositions. The prior art reference generically encompassed the bisphenol A and discloses the three dicarboxylic acids claimed. Although the United States Patent and Trademark Office rejected the claim as obvious over the prior art and the Board affirmed the rejection, the Court reversed the Board's decision. The Court recognized that the prior art reference contained a large number of diphenol derivatives. Baird, 16 F.3d at 383, 29 USPQ2d at 1552. Although it recognized that the prior art encompassed the specific esters when the specific variables were properly chosen, it held that there was no suggestion in the prior art to select the correct variables. Id. In fact, the Court focused on the fact that the preferred embodiments of the prior art related to more complex diphenols than biphenol. Id. It further held that there was no motivation in the prior art reference to select the correct variables to lead to the claimed compounds. Id. In fact, based on the teaching of therein, the Court further held that the reference taught away from the claimed subject matter. Id.

Just like Jones and Baird, Seko, et al. encompasses a disclosure encompassing a large genus. In view of the large number of species encompassed within the prior art reference, and the large number of variables in its genus, there is nothing in the prior art reference which would suggest, among all those possibilities, the selection of the proper combination to lead to the compounds used in the invention. For example, there is no teaching or suggestion in the prior art reference which would suggest motivate one to combine all of the specific variables, i.e., R_1-R_4,

A, E, J and D that would lead to the compounds used in the present invention. Therefore, using the rationale held in In re Baird and In re Jones, the prior art does not provide the requisite motivation for the proper selection of the various variables to lead to a compound falling within the scope of claimed subject matter, and as a consequence, Seko et al. do not teach, disclose or suggest the subject matter in the rejected claims.

The Office Action cites Lowry, et al. Just like the other rejections hereinabove, Lowry et al. do not overcome the deficiency of the prior art. Applicants reiterate the comments of Lowry et al. hereinabove and incorporate the same by reference. Lowry et al. do not teach or disclose any compounds in addition to those in Seko, et al. for treating pain. It is used to support theoretical considerations regarding electing withdrawing groups or election donating groups. Lowry et al. does not comment on which groups affect activity. Lowry et al. does not overcome the deficiency of the primary reference. Thus, the combination of Seko et al. and Lowry et al. do not teach, disclose or suggest the subject matter of the present invention recited in the rejected claims. Thus, the subject matter of Claims 1, 3, 8, 10-19, 73 and 75 under 35 U.S.C. §103 is not rendered obvious by the teachings of Seko et al. in combination with Lowry et al., withdrawal thereof is respectfully requested.

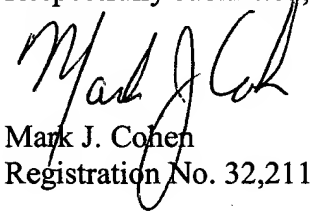
The remaining rejections are rejections under 35 USC §103 and combine the teachings of Lowry individually with Montana, et al., Laruelle, et al., Balasubramanium, et al., Morgan, Fink, Schwender, et al., and Eisenbach-Schwartz, et al., and the combination of Montana, et al. and Konttinen, et al. Lowry is being cited to show that certain groups are electron withdrawing groups or electron donating groups that are electronically different from hydrogen. This relates to a theoretical consideration. Lowry, et al. do not teach, disclose or suggest nor is it being cited for teaching, disclosing or suggesting compounds in addition to those discussed in the primary

reference for treating pain. Applicants reiterate all of the arguments with respect to each of the individual primary references described hereinabove and incorporate the same by reference. Inasmuch as the teachings of Lowry, et al. do not overcome the deficiencies described hereinabove with respect to each of the primary references, the combination of each of the aforementioned references with Lowry do not teach, disclose or suggest the subject matter of the rejected claims. Thus, each the rejections of the claimed subject matter under 35 USC §103, citing each of the primary references with Lowry, et al. is overcome; withdrawal thereof is respectfully requested.

The Office Action has objected to Claim 5, 15, 58-62, and 79-83 for being dependent upon a rejected base claim but has indicated that the subject matter therein would be allowable if placed in independent form. However, in view of the arguments presented hereinabove, the claims are no longer dependent upon a rejected claim. Thus, the objection of Claims 5, 15, 58-62 and 79-83 is overcome, withdrawal thereof is respectfully requested.

Thus, in view of the Amendments and the remarks hereinabove, it is respectfully submitted that the present case is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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